

### **REMARKS**

Claims 1-32 are pending in this application. Claims 1-32 have been rejected in the Office Action dated September 25, 2006. Claims 13, 22, 25 and 27 are objected to because of informalities. By this Amendment, Applicant has amended claims 12-13 and 21-22. Applicant has cancelled claims 1-11, 15-20, and 24-32 without prejudice. Applicant has also added new claims 33-34. Support for the claim amendments and new claims can be found, *inter alia*, at pages 6 to 7, ¶ 23, page 14, ¶¶ 34 and 36, page 19, ¶¶ 45 and 46, and in the specification and claims as originally filed. The amendments introduce no new matter, and thus, their entry is respectfully requested.

#### **Claim Objections**

Claims 13, 22, 25 and 27 were objected to because of informalities. Applicant has either canceled such claims without prejudice or corrected these informalities. Thus, Applicant submits that the objections have been overcome.

#### **Claim Rejections – 35 U.S.C. § 112, first paragraph**

Claims 1-4, 7-9, 15-18 and 24-30 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicant has canceled these claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claims 1-2, 7, 15-16 and 28 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicant has canceled these claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claims 1-2, 5-6, 9-27 and 29-32 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The office

action contends that the above rejected claims lack adequate written description for esters of the claimed compounds. Applicant has either canceled certain of the above rejected claims or amended the remaining claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1-14 and 17-32 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite and for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In response, Applicant has canceled certain of the rejected claims and amended the remaining claims in order to overcome the above rejection. Thus, Applicant respectfully requests that the rejections be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. § 102

Claims 1-12, 15-21, 24 and 26 were rejected under 35 U.S.C. § 102 as being anticipated by Maurer et al., (U.S. Patent No. 6,352,844). In order to expedite prosecution and without conceding correctness of the Office Action's contentions, Applicant has canceled certain of the rejected claims and amended the remaining claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claims 1-12, 15-21, 24 and 26 were rejected under 35 U.S.C. § 102 as being anticipated by Maurer et al., (U.S. Patent No. 6,368,831). In order to expedite prosecution and without conceding correctness of the Office Action's contentions, Applicant has canceled certain of the rejected claims and amended the remaining

claims thereby rendering the above rejection moot. Thus, Applicant respectfully requests that the above rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 13-14, 22-23, 25 and 27 under 35 U.S.C. § 103 as being obvious over Maurer et al., (U.S. Patent No. 6,368,831) in view of Abe et al. The Office Action asserts that use of D-threo-PPMP as a ceramide degradation inhibitor in accordance with the claimed methods and formulations would have been obvious to one of ordinary skill in the art based on the teachings of the cited references.

In order for references to render a claim obvious, the combination of references must disclose each and every element of the claim, there must be a motivation or suggestion to combine the cited references and a reasonable expectation of success for such combination.

Maurer et al. '831 disclose that the racemic mixture, D, L-threo-PPMP, inhibits both glucosylceramide synthase and 1-O-acyceramide synthase and significantly increases the cytotoxicity of 4-HPR (fenretinide). Maurer et al. do not teach or suggest using the isolated enantiomer, D-threo-PPMP, according to the methods or formulations of the present claims.

Further, Abe et al. states that comparison of the two pairs of aliphatic inhibitors (PDMP and PPMP) showed that the 2R,3R (D-threo) form is the primary inhibitor of glucosyltransferase. However, there was relatively small but significant activity in the case of the (erythro) 2R,3S stereoisomer. (p. 615). The Office Action contends that Abe et al., teach that the D-threo-PPMP enantiomer is the more effective inhibitor of glucosylceramide synthase.

Applicant submits, however, there is no teaching, suggestion, or motivation in the above cited references to produce the claimed invention or suggest the desirability of the claimed invention. While Applicant disputes the Office Action's contention that Abe et al. teach that the D-threo-PPMP enantiomer is the more effective inhibitor of glucosylceramide synthase compared to the L enantiomer, even if this were the case it does not teach or suggest that the D-threo-PPMP enantiomer would significantly increase the cytotoxicity of fenretinide according to the claimed invention. Indeed, there is no teaching or suggestion of administering fenretinide and D-threo-PPMP together where "...the ceramide generating retinoid is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide generating retinoid and the ceramide degradation inhibitor when administered separately."

Furthermore, Maurer et al. '831 only discloses the use of the racemic mixture D, L-threo-PPMP for increasing the cytotoxicity of fenretinide and does not teach or suggest the use of an isolated enantiomer, much less the D-threo-PPMP enantiomer, in methods or formulations according to the claimed invention. A person of skill in the art would not have a reasonable expectation of success that the isolated D-threo-PPMP enantiomer would synergistically increase fenretinide cytotoxicity.

Thus, the cited references do not teach or suggest a method or formulation for treating a hyperproliferative disorder in accordance with the amended claims. There is no motivation or suggestion to combine the references and produce the claimed

invention, much less a reasonable expectation of success. Thus, Applicants respectfully request that the above rejection be reconsidered and withdrawn.

#### Double Patenting

Claims 1-12, 15-21, 24 and 26-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 20-23 of Maurer et al., (U.S. Patent No. 6,368,831). In order to expedite prosecution and without conceding correctness of the Office Action's contentions, Applicant has canceled certain of the rejected claims and amended the remaining claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

Claims 1, 4-6, 12, 15, 21, 23, 24, and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of Maurer et al., (U.S. Patent No. 6,352,844). In order to expedite prosecution and without conceding correctness of the Office Action's contentions, Applicant has canceled certain of the rejected claims and amended the remaining claims, thereby rendering the above rejection moot. Thus, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

In view of the foregoing, it is submitted that the claims are in condition for allowance. A Notice of Allowance is requested.

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Respectfully submitted,

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